

Public Health and Medical Humanities History Corner

Robert J. Levine: a distinguished problem solver



ROBERTO BUCCI⁽¹⁾, SERENA TRAGLIA⁽¹⁾

(1) Università Cattolica del Sacro Cuore School of Medicine, Rome, Italy

CORRESPONDING AUTHOR: Roberto Bucci, Università Cattolica del Sacro Cuore School of Medicine, Largo Francesco Vito, 1, 00168 Rome, Italy. e-mail: rbucci@rm.unicatt.it

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ABSTRACT

Robert Levine: a man capable of intelligent and constructive criticism, who could accept with humility the criticisms of others. A man who left a deep mark in the history of research, both inside and outside the United States. Above all, a great problem solver.

A brilliant doctor and refined bioethicist, he was able to deal with the disasters of research on human subjects and to remedy to them. He fought against the application in clinical practice of ethical principles valid only for research, but also against the universalisation of the rules of informed consent, which are applicable only to Western cultures. A researcher who deserves to be known by all, especially by young people.

In the early 70's research in the US was in the thick of a heated public debate. Most criticisms came from within the medical profession. In 1966 it appeared in the New England Journal of Medicine an article, written by Henry Beecher, who found in medical literature almost twenty cases of apparent violation of fundamental human rights [1].

The earliest of these cases was reported in 1970, while in progress, uninterrupted since 1932, in Tuskegee, Alabama. From 1932 to 1972, 600 black sharecroppers in Alabama (U.S. State with a high proportion of African-Americans) were enrolled in a study authorised by the Public Health Service of the United States, with the purpose of observing the natural course of syphilis when not treated. Patients enrolled were kept ignorant of their illness, and were only told they needed to

be kept under observation due to “bad blood.” Of the 600 people enrolled, 399 were syphilitic and 201 healthy individuals (as a control group).

The syphilitic were not told that they were participating in a non-therapeutic experiment, and were further misled to undergo regular “lumbar punctures” under the deception that they were receiving “free special treatment” for their bad blood.

Consent was obtained with no effort. Patients enrolled were living in social deprivation and manipulation was very easy. During the whole period of the experiment, lasted for forty years, the patients were intentionally and systematically deprived of actual health care assistance, even when, in the mid 40’s, penicillin, the first effective antibiotic against syphilis, had become available in the US.

The study went on until 1972 when it was denounced on the front page of the New York Times. A committee appointed by the Department of Health, Education and Welfare concluded, in 1973, that the study was not unethical and prevented its continuation [2, 3].

The scientific community regarded it as a bitter question.

Other unethical experiments were perpetrated, in the same time lapse, on children with severe mental illness at the Willowbrook State School in New York. In an attempt to develop effective prophylactic treatments against hepatitis, a paediatrician infected with isolated virus about 700-800 children between 1956 (when the study was started), and 1970 (when the research came to the attention of the media).

The module used to obtain consent from parents or guardians was written in a way as to lead the signatory to believe that children might not be welcomed in hospital for future treatments if they had not participated in the research project [4].

Tuskegee and Willowbrook are the two best-known examples, but several other cases were emerging, and public confidence in researchers suffered a heavy blow. It was time to make explicit the rules to govern clinical research: these so-called scientific studies were being carried out legally in the United States, a society that prided itself of being democratic and avant-garde in the promotion of human rights. In fact, civil and scientific society came gradually to recognize that legal rules were necessary to ensure the full protection of human subjects in scientific studies.

The two studies reported here led to the suspicion that more similar episodes might also be occurring elsewhere in the so-called civilized, democratic part of the world - in fact, that Tuskegee and Willowbrook were only the tip of the iceberg, and that professional misconduct in ethics might be spread among health-care workers. A thorough analysis of this unfortunate reality led to share the knowledge that there was a real lack of integration between the world of scientific facts and that of ethical values.

In this context, the U.S. Congress convened a scientific commission to draft the “National Commission for the protection of human subjects of biomedical and behavioural research”. The Commission worked from 1974 to 1978. The best scientists of the time were involved to deal with such an intricate issue that threatened to jeopardize the future of research in the country all together [5].

Robert J. Levine, member of the Committee and Chief of the Section of Clinical Pharmacology at Yale University School of Medicine, played a key role. Due to his prestige and scientific level Robert Levine was a special member at special conditions. He was asked since 1974 to join the staff of the Commission. He had already started to write about the regulations that the Federal Department of Health, Education and Welfare were proposing as regulations for the protection of human research subjects. Levine had a very negative opinion about these proposals and been very vocal on his criticism through editorials, scientific symposia and position papers.

When asked to join the Committee staff, he refused on the grounds that he would

be accepting an honorary from the federal government, which would somehow conflict with his liberty of criticising the government at the same time. Levine's cooperation was finally obtained by nominating him "special consultant," on a 90 percent of the salary the other members were receiving, which meant he was still free to criticise whenever he saw fit.

Also, he did not have to move to Washington and continued to live and teach at the University of Yale. His work for the commission, however, was very conspicuous: many of the final statements of the report were taken from his essays in that period, after being submitted to the Commission for discussion.

Levine described his time with the Commission as "a marvellous experience". "It was kind of like being a post-doctoral student in bioethics, with the best and the brightest mind of the country serving as your dissertation committee, because all the papers I wrote - what the Commission called their 'background theoretical essays' - were sent out to philosophers, lawyers, surgeons, nurses all over the country who then criticized my work. And then I got to work again with it".

He accepted with the typical humility of the great mind all the critical remarks he received and could so improve his work. Most of the very large appendix to the Belmont Report is the papers he wrote in those circumstances.

Setting up a Commission proved to be the right move by the government. It blocked the spiral of accusations that threatened to undermine forever the relationship between researchers and the public.

The Commission worked on four main nodes: the boundaries between biomedical research and the practice of medicine, the evaluation of risk-benefit criteria in research that includes human subjects, the elaboration of appropriate guidelines for the selection of experimental subjects participating in this research, the nature and the definition of "informed consent" in various areas of research.

The result of the work, which took four years, is condensed into a document: Ethics Principles and Guidelines for the Protection of Human Subjects of Research, also known as the Belmont Report (from the Belmont Conference Centre of the Smithsonian Institution, where a conference that outlined the terms of such report was organized in February 1976). The Belmont report has become a mainstay of research ethics. In it three standard principles of bioethics were identified as criteria for assessing the quality of research ethics: respect for personal autonomy, justice and beneficence.

Furthermore, the requirement of "informed consent" was also introduced as a necessary legal condition in research. The Institutional Review Boards were created to control and promote a new culture of clinical research. The clinical researchers were explicitly forbidden to take unilateral decisions on the ethics of their research, and were compelled to share with their colleagues the obligation to follow the same guidelines.

Reluctance to trust the researchers and the desire to protect the well-being of trial subjects produced not only new rules for research, but new rules for medicine as a whole.

In other countries, government committees were created like the U.S. National Commission to address issues related to the progress of medicine and biology. Many of them made the depressing experience to see their work end up locked in a dead drawer of politicians and decision makers.

The report from the US National Commission had quite an opposite fate: it was successful. Maybe too much so... It just sounds paradoxical but it was the very Robert Levine to criticise his own creature.

Instead of rejoicing, Robert Levine was aware of the shadows of this success, almost as if he shared the fear of possible accusations of ethical imperialism: the American model seeking to impose itself over other possible approaches. When the CIOMS (Council for International Organizations of Medical Sciences, based in Geneva) asked him to develop a definition of informed consent format

that could be applied to different countries and cultures, Levine criticised the universal validity of the Western model.

Our concept of informed consent depends on how we think of the person, saying that every individual has the same value, dignity and the right to equal respect and consideration. This vision of human rights as universally valid - on which, ultimately, is based on self-determination and the doctrine of informed consent - goes in the same direction. This approach leads to impose the same ethical standards in the conduct of research: in America, Africa and Asia, in developed countries as well as those in the developing world.

The problem was not abstractly and theoretically founded, but very practical. Research crosses over national borders. The universalist perspective has indisputable points in its favour: considering human rights as valid everywhere, it defends people against possible exploitation (by, for example, a multinational drug industry, which could be tempted to take advantage of people without protection). But we cannot ignore the violence inherent the adoption of a single, Western model throughout the world. In some cultures, specific categories of people are by tradition dominant. In many countries, for example, women are not entitled to take legal decisions without their husbands' or fathers' consent. In other cultures there are prevailing groups; some people are too illiterate and lack any form of education so that they do not have the requirements to give consent as required in the Western model. Excluding all of them from research, not just from its risks but also from its advantages - is it a matter of justice and ethics, or simply an abuse? Informed consent should be sought after through models separated from international standard but without suspects of lesser quality ethics.

There was also a much more serious reason why Robert Levine was worried for the great success of the Belmont Report. Due to an unfortunate misunderstanding, the research ethics regulations produced in Belmont overlapped clinical ethics tout court.

Levine moved from a general observation: the relationship between doctor and patient was increasingly deteriorating. When all doctors could do was holding hands with the child who died of diphtheria, everyone seemed to be satisfied. Today doctors can administer powerful and very effective antibiotics, after a few days the child is back to play with other children in the yard, but people are dissatisfied with the doctor. What happened in this relationship?

Levine identified a reason for the deterioration in the highly successful image of ethics in clinical research. He realized that his ethics manual, aimed at the regulation of clinical research, was being used in medical schools to teach medical ethics, as if the rules established to obtain informed consent in experimental conditions could apply in cases where the doctor and the patient should take one decision, big or small, about the patient's life, health or well-being [1].

Ethical rules governing research are applicable for scientists who carry out their research on human subjects. To limit researcher power, the Belmont language of rights and duties was appropriate: it is the right language for regular procedures between opponents. Or at least among strangers [6].

But this is not the kind of relationship we want in a doctor-patient relationship. Could anyone imagine a friendship that begins with the declaration of rights and freedom? We want a friend to treat us fairly, to be sure, but we want above all to be considered in our uniqueness as special beings. And we want exactly the same from a clinician.

For this type of relationship analysis problems that bioethics has developed for research is out of place. Indeed, it is deforming because it gives a strong emphasis on strict rules, promotes a minimalist view of ethics, while decisions whether to accept or reject the treatments are related to the duration and to the quality of life of patients. They demand a kind of reasoning which does

not derive, simply, by rules and regulations, but from the understanding of the context and of the place that the individual occupies, from his/her family ties and from the community elements involved. This is the kind of doctor we want as personal physician.

This is also why Robert Levine developed for medical students at Yale University a 40-hour course which he called “professional responsibility”, a course that is compulsory for all first year students. Those who want to become doctors must learn to have a good relationship with their patients. A good doctor cannot just make the patient sign an informed consent form.

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